JOC The Journal of Organic Chemistry

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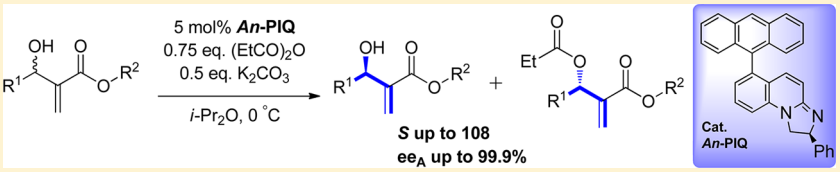
# Kinetic Resolution of α-Methylene-β-hydroxy Esters Catalyzed by Acyl Transfer Catalyst *An*-PIQ

Shan-Shan Jiang, Qin-Chang Xu, Ming-Yu Zhu, Xingxin Yu,* and Wei-Ping Deng*

Shanghai Key Laboratory of New Drug Design, School of Pharmacy, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, P. R. China

Supporting Information




**ABSTRACT:** A highly efficient nonenzymatic kinetic resolution of a series of structurally diverse racemic α-methylene-β-hydroxy esters utilizing the acyl transfer catalyst *An*-PIQ and propionic anhydride is reported. This procedure provides recovered alcohols with extremely high ee's (up to >99%) in reasonable conversions and excellent selectivity factors (*S* up to 108). Several synthetically important substrates were resolved in gram-scale reactions, and highly optically pure α-methylene-β-hydroxy esters were obtained with excellent *S* values and good yields.

## INTRODUCTION

Kinetic resolution (KR) via nucleophilic acyl transfer catalysis is one of the most powerful and efficient strategies to obtain optically pure compounds.[1] Since the pioneering work of Vedejs[2a,b] and Fu[2c−e] on the nonenzymatic KR of secondary alcohols, using chiral phosphine and chiral 4-dimethylaminopyridine (DMAP) analogues as catalysts, respectively, asymmetric nucleophilic acyl transfer catalysis for the KR of a variety of secondary alcohols has been further developed.[3] It is worth noting that the amidine-based nucleophilic catalysts reported by Birman,[4] such as $CF_3$-PIP,[4a] Cl-PIQ,[4b] BTM,[4c] and HBTM,[4d,e] exhibited excellent tolerance to substrate scope, which can be attributed to π−π and π−cation interactions between the $sp^2$ functional groups of the substrates and acylated catalysts, affording high selectivity factors. Through combination of the key features of both Fu's and Birman's catalysts, a new variant of nucleophilic catalyst has been designed, Fc-PIP,[5a] for the KR of arylalkyl carbinols (*S* up to >1800) in our group. Although much effort has been devoted to the development of nonenzymatic catalysts for the KR of a variety of secondary alcohols,[4f,6] to the best of our knowledge, their application for the KR of α-methylene-β-hydroxy esters (Morita−Baylis−Hillman adducts, MBH adducts) by acylation has received much less attention. In 2007 Connon[7] reported the only example of nonenzymatic acylative KR of MBH adducts derived from aromatic aldehydes. However, very low selectivity (*S* = 13) was obtained, probably due to the intrinsic flaw of two planar $sp^2$-hybridized substituents. More than that, a nucleophilic nonenzymatic acylative KR of aliphatic aldehyde-derived MBH adducts is unknown; thus, a great challenge still remains.

MBH adducts are densely functionalized molecules (e.g., **MBH-1** or **MBH-2**) and consequently are highly versatile chiral building blocks,[8,9] which have been widely employed for the synthesis of important optically pure natural products and bioactive compounds (Figure 1). Therefore, much effort has been devoted to develop a highly efficient asymmetric MBH reaction for the preparation of optically pure or enantioenriched α-methylene-β-hydroxy esters.[10,11] Notably, Hatakeyama[11a] developed a highly enantioselective MBH reaction of aldehydes using β-isocupreidine (β-ICD) as the chiral amine

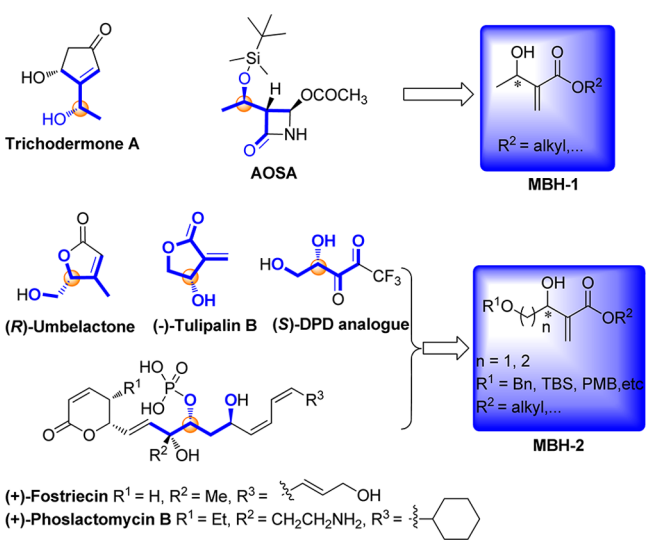



**Figure 1.** Natural products and important synthetic intermediates obtained from optically pure MBH adducts.

**Received:** January 12, 2015
**Published:** February 18, 2015





DOI: 10.1021/acs.joc.5b00073
J. Org. Chem. 2015, 80, 3159−3169

catalyst, and hexafluoroisopropyl acrylate (HFIPA) as the activated alkene, and afforded the corresponding MBH adducts in up to 99% ee. However, the efficient $\beta$-ICD−HFIPA protocol still suffers from the formation of a large quantity of dioxanone byproducts, especially when aliphatic aldehydes are used as electrophiles.

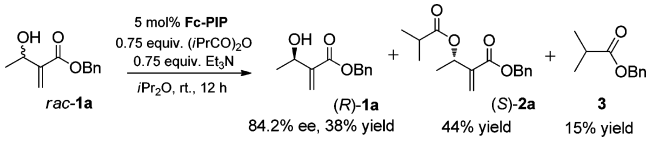
We recently synthesized a highly efficient nucleophilic catalyst *An*-PIQ[5b] for the KR of arylalkyl carbinols, with excellent selectivity factors (up to 530). Considering the current difficulties in the preparation of optically pure $\alpha$-methylene-$\beta$-hydroxy esters, we set out to design suitable substrates and apply our developed catalysts in the KR of racemic MBH adducts, derived from aliphatic aldehydes and acrylates. However, several challenges are associated with this procedure: (1) the choice of the suitable ester group, (2) the relationship between individual $\pi-\pi$ interaction of the alkene and carbonyl group with the acylated catalyst, and (3) the role of *An*-PIQ structure and whether it is decisive for the selectivity factor. In order to address these issues and surmount the difficulties in preparation of optically pure $\alpha$-methylene-$\beta$-hydroxy esters, a series of PIQ analogues and MBH adducts were synthesized to test the feasibility.

Herein, we report a highly efficient nonenzymatic KR of racemic $\alpha$-methylene-$\beta$-hydroxy esters utilizing the acyl transfer catalyst *An*-PIQ. This protocol provides recovered alcohols with extremely high ee values (≥99%) and in reasonable conversions and good-excellent selectivity factors (*S* up to 108).

## RESULTS AND DISCUSSION

Initially, *rac*-**1a** was used as the substrate to test the feasibility of the KR with Fc-PIP[5a] as the nucelophilic catalyst, which is a useful catalyst for the KR of arylalkyl carbinols. The reaction proceeded tediously when isobutyric anhydride was used as the acylating agent in diisopropyl ether at room temperature for 12 h, providing unreacted (*R*)-alcohol (yield: 38%; ee: 84.2%), (*S*)-acylated product **2a** (yield: 44%; ee not determined), and small quantities (15% yield) of byproduct **3** (Scheme 1). It is obvious that benzyl ester **1a** is not stable enough in the presence of Fc-PIP.

**Scheme 1. Fc-PIP-Catalyzed KR of $\alpha$-Methylene-$\beta$-hydroxy Esters 1a**




In order to solve this problem, benzhydryl ester **1b** was used instead of **1a**. To our delight, the reaction proceeded much smoothly and provided unreacted **1b** and acylated **2b** in 43.7% ee and 83.1% ee, respectively, with a slightly higher selectivity factor ($S$ = 17) compared with Connon's[7] report. Encouraged by this result, *rac*-**1b** was then chosen as the model substrate to investigate the catalytic asymmetric KR capability of different nucleophilic catalysts (Figure 2).[4b,5] As shown in Table 1, it was surprising that our newly developed catalyst *An*-PIQ gave the optimal selectivity factor ($S$ = 38) (Table 1, entry 2), whereas other catalysts such as Cl-PIQ displayed lower *S* values (Table 1, entries 3−5). The selectivity factor $S$ = 38 given by *An*-PIQ is already the best result in the nonenzymatic KR of a MBH adduct, and this exhibits potential practical utility for the synthesis of optically pure MBH adducts, which prompted us to further optimize the reaction system.

Screening solvents (Table 2, entries 1, 4−11) revealed that diisopropyl ether ($S$ = 56) gave, in general, an *S* value higher than that of other solvents. Nevertheless, toluene and other ethers (e.g., diethyl ether, methyl *tert*-butyl ether (MTBE), and cyclopentyl methyl ether (CPME)) showed similar selectivities (entries 4, 5, 6, 9) to those of diisopropyl ether. Our screening of anhydrides revealed that propionic anhydride was optimal, affording an excellent selectivity factor $S$ = 89 (entries 12 vs 1, 13). An increase in the substrate concentration, to 0.4 M, was found to be detrimental to the selectivity factor (entries 2 and 3). We then examined the effect of bases on the selectivity factor of the KR and found that potasium carbonate gave the optimal result, whereas $Et_3N$, DIPEA (*N*,*N*-diisopropylethylamine), and 2,6-lutidine were found to be slightly inferior to potassium carbonate in terms of both stereoselectivities and conversions (entries 15 vs 12, 14, 16).

Optimization of solvents, anhydrides, bases, and concentrations led us to establish that 5 mol % of *An*-PIQ/$(EtCO)_2O$ (0.75 equiv)/$K_2CO_3$ (0.5 equiv)/$iPr_2O$ (0.1 M)/0 °C were the optimal reaction conditions for catalytic KR of *rac*-**1b**. Under these conditions, this protocol was investigated with different MBH adducts as substrates, and the results are summarized in Table 3. The KR of most benzhydryl esters **1b−i** proceeded smoothly, providing excellent selectivity factors (up to 108) (Table 3, entries 1−8) and extremely high ee values (up to 99.9%) for unreacted alcohols at acceptable conversion ratios. The bulkier alkyl groups ($R^1$) gave lower selectivity factors and reactivities (entries 6, 7). To better understand the role of the benzhydryl group on the selectivity factor, we examined a variety of substrates (**1j−l**) without the benzhydryl ester as $R^2$ group. It was found that all these substrates gave dramatically lower *S* values (entries 9−11) compared with **1i** and **1b**, which indicated the crucial effect on stereoselective differentiation by the benzhydryl group. Next, a series of structurally challenging and synthetically versatile $\alpha$- or $\beta$-functionalized MBH adducts **1m−p** were also employed for this asymmetric KR (Table 3, entries 12−15); if successful, this would afford optically pure chiral building blocks for the synthesis of bioactive natural products, such as tulipalin B, umbelactone, (+)-fostriecin,

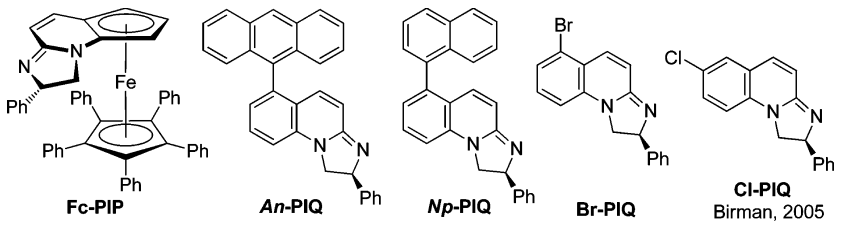
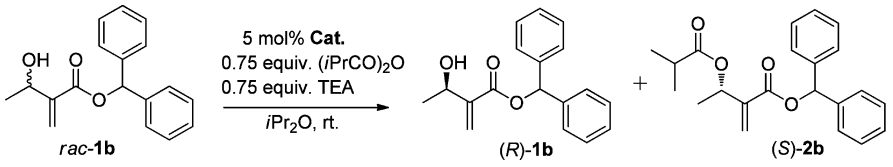



**Figure 2.** Nucleophilic catalysts.



DOI: 10.1021/acs.joc.5b00073
J. Org. Chem. 2015, 80, 3159−3169

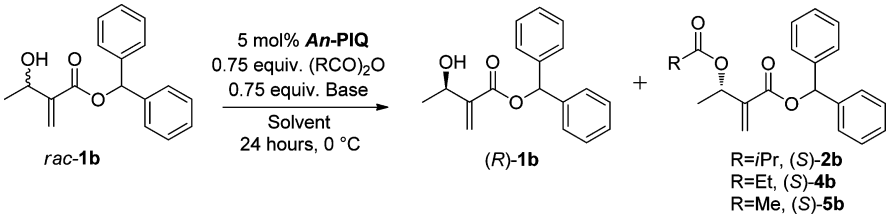
**Table 1. Screening of Catalysts in the KR of (±)-MBH Adduct 1b[a]**




| entry | catalyst | $t$ (h) | **1b** $ee_A$ (%)[b] | **2b** $ee_E$ (%)[c] | $C_{HPLC}$ (%)[d] | $S$ |
|---|---|---|---|---|---|---|
| 1 | Fc-PIP | 6 | 43.7 | 83.1 | 34.5 | 17 |
| 2 | *An*-PIQ | 5 | 65.1 | 90.2 | 41.9 | 38 |
| 3 | *Np*-PIQ | 4 | 66.3 | 81.8 | 44.8 | 20 |
| 4 | Br-PIQ | 18 | 46.2 | 73.2 | 38.7 | 10 |
| 5 | Cl-PIQ | 18 | 54.7 | 58.9 | 48.2 | 7 |

[a]Conditions: Substrate concentration 0.1 M, $(i\text{PrCO})_2O$ 0.75 equiv, $Et_3N$ 0.75 equiv, catalyst 5 mol %. [b]The ee value of the alcohol. [c]The ee value of the ester. [d]The conversion is calculated from the ee values of the ester (*S*)-**2b** and unreacted alcohol (*R*)-**1b**.

**Table 2. Screening of Solvents, Anhydrides Bases, and Concentrations[a]**




| entry | solvent | $(RCO)_2O$ | base | **1** $ee_A$ (%) | $ee_E$ (%) | $C_{HPLC}$ (%) | $S$ |
|---|---|---|---|---|---|---|---|
| 1 | $iPr_2O$ | *i*Pr | $Et_3N$ | 87.4 | 90.3 | 49.2 | 56 |
| 2[b] | $iPr_2O$ | *i*Pr | $Et_3N$ | 95.2 | 85.4 | 52.7 | 47 |
| 3[c] | $iPr_2O$ | *i*Pr | $Et_3N$ | 94.8 | 81.0 | 53.9 | 35 |
| 4 | $Et_2O$ | *i*Pr | $Et_3N$ | 70.3 | 91.9 | 43.3 | 50 |
| 5 | MTBE | *i*Pr | $Et_3N$ | 73.5 | 91.4 | 44.6 | 49 |
| 6 | CPME | *i*Pr | $Et_3N$ | 58.5 | 92.9 | 38.6 | 49 |
| 7 | THF | *i*Pr | $Et_3N$ | 29.2 | 87.8 | 25.0 | 20 |
| 8 | $CH_3CN$ | *i*Pr | $Et_3N$ | 10.7 | 51.7 | 17.2 | 3 |
| 9 | toluene | *i*Pr | $Et_3N$ | 65.5 | 91.9 | 41.6 | 47 |
| 10 | $CHCl_3$ | *i*Pr | $Et_3N$ | 10.7 | 78.9 | 11.9 | 9 |
| 11 | DCM | *i*Pr | $Et_3N$ | 9.8 | 75.9 | 11.4 | 8 |
| 12 | $iPr_2O$ | Et | $Et_3N$ | 97.6 | 90.6 | 51.9 | 89 |
| 13 | $iPr_2O$ | Me | $Et_3N$ | 80.2 | 84.2 | 48.8 | 29 |
| 14 | $iPr_2O$ | Et | DIPEA | 92.2 | 92.6 | 49.9 | 86 |
| 15 | $iPr_2O$ | Et | $K_2CO_3$ | 98.5 | 90.5 | 52.1 | 97 |
| 16 | $iPr_2O$ | Et | 2,6-lutidine | 91.0 | 93.0 | 49.5 | 88 |
| 17[d] | $iPr_2O$ | Et | $K_2CO_3$ | −86.3 | −88.3 | 49.4 | 45 |

[a]Conditions: Substrate concentration 0.1 M, 0.75 equiv of $(i\text{PrCO})_2O$, 0.75 equiv of $Et_3N$, 5 mol % of *An*-PIQ. 0.2 mmol of substrate scale. [b]Substrate concentration 0.2 M. [c]Substrate concentration 0.4 M. [d](*R*)-BTM[4c]as the catalyst.

(+)-phoslactomycin B, and DPD analogues (Figure 1). Surprisingly, α-benzyloxy-substituted **1m** gave an extremely low selectivity factor ($S$ = 3), probably due to a competitive oxygen−cation interaction between the benzyloxy oxygen atom and the carbonyl oxygen atom with the acylated *An*-PIQ.

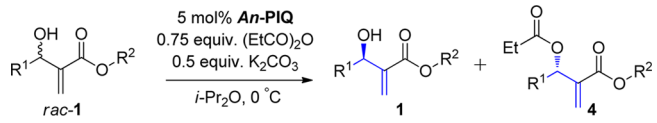
According to Shinna's reports,[12] a carbonyl oxygen−cation interaction was proposed to account for the high selectivity factor in the KR of racemic 2-hydroxyalkanoates (Scheme 2). If it is true, we envisaged that a sterically bulky protecting group instead of benzyl would decrease or even avoid this competition, which would therefore lead to a higher stereoselectivity. As expected, a TBS-protected substrate **1n** was found to be suitable for the KR, affording a dramatically improved $S$ value of 37. In order to further confirm the existence of this hypothetical competitive oxygen−cation interaction between the benzyloxy oxygen atom or the carbonyl oxygen atom and the acylated *An*-PIQ, substrate **1o**, with one more carbon than **1m**, was subjected to the KR and found to give an improved $S$ value equal to 24, providing corresponding unreacted (*R*)-**1o** in 99.1% ee. To our delight, a TBS-protected substrate **1p** gave an excellent selectivity factor ($S$ = 75), which was comparable to that of substrates **1d−f** with longer alkyl chains.

In order to further demonstrate the utility of this protocol, substrates **1b**, **1n**, **1p**, **1o** were chosen for scaled-up investigations as shown in Scheme 3. The reactions proceeded smoothly for all cases, to afford the unreacted alcohol (*R*)-**1b**, (*S*)-**1n**, (*R*)-**1p**, (*R*)-**1o** in over 99.0% ee with good to excellent selectivity factors ($S$ = 20−82). (*R*)-**1b** and (*R*)-**1o** were then subjected to transesterification to provide the corresponding methyl esters (*R*)-**6** and (*R*)-**7** in 81% and 86% yield, respectively, which can be used for the synthesis of some



DOI: 10.1021/acs.joc.5b00073
J. Org. Chem. 2015, 80, 3159−3169

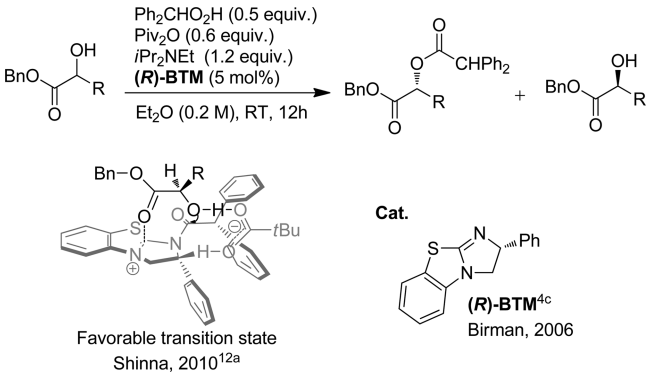
**Table 3. Scope and Generality of the *An*-PIQ-Catalyzed KR[a]**




| entry | $R^1$ | $R^2$ | no. | **1** $ee_A$ (%) | **4** $ee_E$ (%) | $C_{HPLC}$ (%)[b] | $S$ | $C_{AVG}$ (%)[d] | $S_{AVG}$[d] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Me | $CHPh_2$ (**1b**) | 1 | 99.4 | 88.1 | 53.0 | 90 | 52.6 | 94 |
| | | | 2 | 98.5 | 90.5 | 52.1 | 97 | | |
| 2 | Et | $CHPh_2$ (**1c**) | 1 | 94.7 | 90.7 | 51.1 | 75 | 51.5 | 76 |
| | | | 2 | 96.5 | 89.9 | 51.8 | 76 | | |
| 3 | *n*Pr | $CHPh_2$ (**1d**) | 1 | 98.4 | 87.6 | 52.9 | 72 | 53.4 | 74 |
| | | | 2 | 99.6 | 85.3 | 53.9 | 76 | | |
| 4 | *n*Bu | $CHPh_2$ (**1e**) | 1 | 97.6 | 89.4 | 52.2 | 78 | 52.4 | 80 |
| | | | 2 | 98.3 | 89.1 | 52.5 | 82 | | |
| 5 | *i*Bu | $CHPh_2$ (**1f**) | 1 | 99.9 | 84.8 | 54.1 | 90 | 53.8 | 99 |
| | | | 2 | 99.9 | 87.2 | 53.4 | 108 | | |
| 6 | *i*Pr | $CHPh_2$ (**1g**) | 1 | 62.9 | 90.8 | 40.9 | 40 | 40.8 | 40 |
| | | | 2 | 62.5 | 91.0 | 40.7 | 40 | | |
| 7 | *c*Hex | $CHPh_2$ (**1h**) | 1 | 65.0 | 87.5 | 42.6 | 29 | 42.4 | 29 |
| | | | 2 | 63.8 | 87.7 | 42.1 | 29 | | |
| 8[c] | $PhCH_2CH_2$ | $CHPh_2$ (**1i**) | 1 | 99.4 | 80.8 | 55.2 | 53 | 54.9 | 56 |
| | | | 2 | 99.4 | 82.6 | 54.6 | 59 | | |
| 9 | $PhCH_2CH_2$ | Me (**1j**) | 1 | 73.2 | 79.1 | 48.1 | 19 | 47.7 | 20 |
| | | | 2 | 72.1 | 80.4 | 47.3 | 20 | | |
| 10 | Me | $CH_2$-1-naphthyl (**1k**) | 1 | 61.8 | 84.0 | 42.4 | 22 | 42.2 | 22 |
| | | | 2 | 60.9 | 84.5 | 41.9 | 22 | | |
| 11 | Me | $CH_2CH_2Ph$ (**1l**) | 1 | 77.9 | 90.9 | 46.2 | 50 | 46.8 | 50 |
| | | | 2 | 81.3 | 90.4 | 47.4 | 50 | | |
| 12 | $BnOCH_2$ | $CHPh_2$ (**1m**) | 1 | 54.2 | 35.2 | 60.6 | 3.4 | 63.0 | 3 |
| | | | 2 | 55.4 | 29.4 | 65.3 | 3.0 | | |
| 13 | $TBSOCH_2$ | $CHPh_2$ (**1n**) | 1 | 85.2 | 86.2 | 49.7 | 37 | | 37 |
| 14 | $BnOCH_2CH_2$ | $CHPh_2$ (**1o**) | 1 | 99.1 | 65.0 | 60.4 | 24 | | 24 |
| 15 | $TBSOCH_2CH_2$ | $CHPh_2$ (**1p**) | 1 | 95.7 | 90.2 | 51.5 | 75 | | 75 |

[a]Conditions: 0.1 M substrate concentration, 0.75 equiv of $(EtCO)_2O$, 0.5 equiv of $K_2CO_3$, 5 mol % of *An*-PIQ, 24 h. [b]Calculated from the ee of the ester and unreacted alcohol. [c]22 h. [d]The average value of the two results.

**Scheme 2. Proposed Transition State by Shinna[12a]**



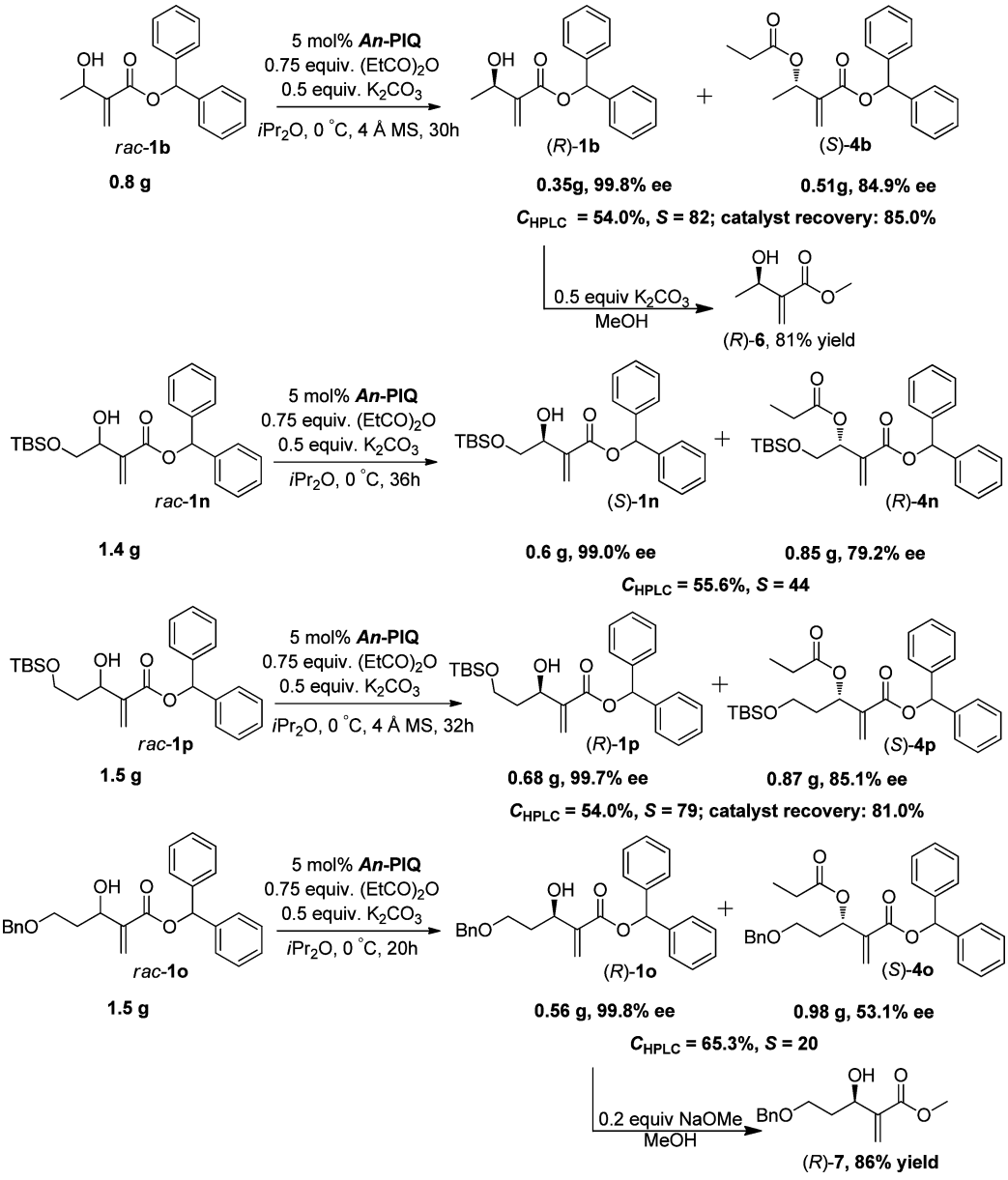

bioactive natural products as shown in Figure 1. For the KR of **1b** and **1p**, the catalyst *An*-PIQ was recovered in over 80% yield and without loss in activity in the next KR process. The absolute configurations of optically active **1b** was determined by comparing the optical rotation (our synthetic **6**: $[\alpha]^{25}_D$ = +17.4°, *c* 0.01, $CHCl_3$, reported $[\alpha]^{25}_D$ = +10.2°, *c* 0.8, $CHCl_3$) and HPLC data for methyl ester **6** with that in the literature[8d,13] and confirmed as *R*. Considering the structural diversity, the optical rotation of our synthetic **1j** was determined (72.1% ee, $[\alpha]^{25}_D$ = +24.9°, *c* 0.01, $CHCl_3$; reported 98% ee, $[\alpha]^{22}_D$ = +28.1°, *c* 0.83, $CHCl_3$), and its absolute configuration was accordingly confirmed as *R* in comparison with the sign of optical rotation from the literature report.[11d] Furthermore, the simple transesterification of our synthetic **1i** provided **1j**, and the sign of its optical rotation was found the same as that of **1j** derived from KR from Table 3 ($[\alpha]^{25}_D$ = +26.8°, *c* 0.01, $CHCl_3$), which established the absolute configuration of our synthetic **1i** as *R*. With the above three examples for establishing the absolute configuration of our synthetic alcohols as *R* configurations, the absolute configurations of the remaining cases can be deduced accordingly by a similar manner of steric control.

According to the results above, we speculated that benzhydryl group has a major effect on the enantioselectivity of the asymmetric KR, in collaboration with the carbonyl group of the substrate. However, it is still not clear whether the terminal double bond has a similar effect on enantioselectivity. Therefore, a substrate without a carbon−carbon double bond (**1q**) was prepared and used to investigate the role of the double bond (Scheme 4). Notably, the selectivity factor ($S$ = 24) of **1q** dramatically decreased compared to that of the substrate **1b** ($S$ = 97). This implies that the carbon−carbon double bond plays an important role in $\pi-\pi$ interaction between the substrate and the acylated *An*-PIQ. Considering all the above-mentioned parameters, a hypothetical transition state was proposed, in which the high selectivity can be attributed to $\pi$−cation interactions between the conjugated $\alpha,\beta$-unsaturated

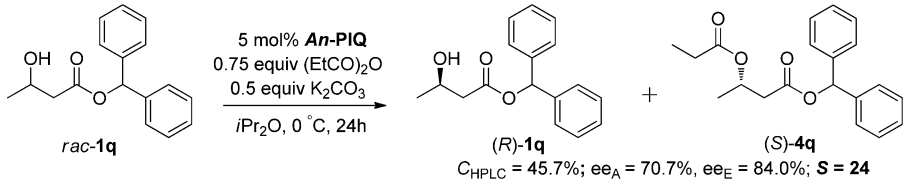


DOI: 10.1021/acs.joc.5b00073
J. Org. Chem. 2015, 80, 3159−3169

**Scheme 3. Larger Scale Catalytic KR of Important Intermediates of Active Natural Products**




**Scheme 4. Investigation of the Substrate without a Carbon−Carbon Double Bond**




ester and the acylated *An*-PIQ, as well as a $\pi-\pi$ stacking interaction between one phenyl ring of benzhydryl group and the anthranyl group (Figure 3).

## CONCLUSION

In conclusion, we have developed a highly effective non-enzymatic acylative KR of racemic $\alpha$-methylene-$\beta$-hydroxy esters with different alkyl side chains by use of the acyl transfer catalyst *An*-PIQ and propionic anhydride, providing recovered alcohols with extremely high ee's (up to >99%) in reasonable conversions and excellent selectivity factors ($S$ up to 108). This work complements the asymmetric MBH reaction, especially for substrates derived from aliphatic aldehydes. This method was also successfully applied to the KR on gram-scale of important building blocks of several bioactive compounds, and the corresponding optically pure $\alpha$-methylene-$\beta$-hydroxy esters were obtained with excellent ee values. In addition, this protocol makes a breakthrough in the acylative KR of MBH adducts containing the crucial benzhydryl ester. The high selectivity is attributed to the combined interaction of double



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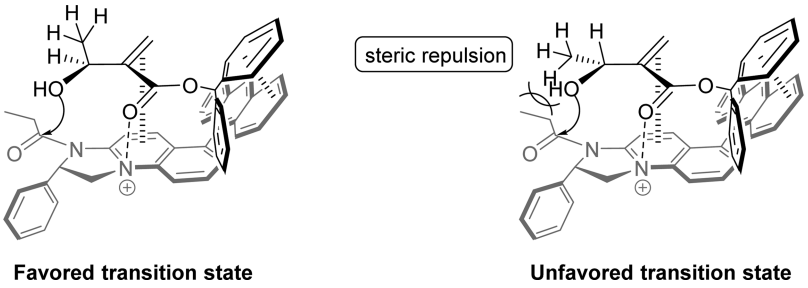



**Figure 3.** Possible transition state for catalyst *An*-PIQ interacting with **1b**.

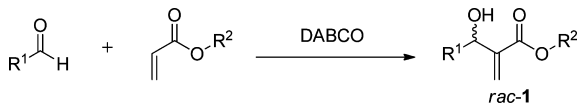
bond, carbonyl group, and phenyl group of substrates with an acyl ammonium intermediate. Further applications of the products and mechanistic elucidation of the chirality induction are ongoing in our laboratory.

## EXPERIMENTAL SECTION

**General Information.** All reagents and starting materials were obtained commercially and used as received unless otherwise stated. Solvents and reagents were dried in advance. Catalyst *An*-PIQ, *Np*-PIQ, Br-PIQ, Fc-PIP, (*S*)-Cl-PIQ, and (*R*)-BTM were synthesized according to literature procedures.[4b,5] $^1$H NMR spectra were recorded on a 400 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The spectra are interpreted as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad single, coupling constant(s) in hertz, and relative integrations are reported. $^{13}$C NMR spectra were recorded on a 400 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard.

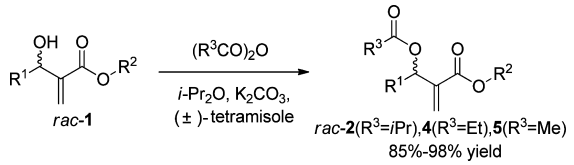
Methods used for kinetic resolution experiments determination of ee's and calculation of conversions and selectivities were adopted from previously published work.[5] Enantiomeric excess values were determined by analysis of HPLC traces, obtained by using chiralpak AD-H, AS-H, OD-H, OJ-H, or IF-H columns with hexane and 2-propanol or EtOAc as solvents. Selectivity factors and conversions were calculated from the enantiomeric excess values of the ester products and the recovered unreacted alcohol substrates according to Kagan's equations.[14,15]

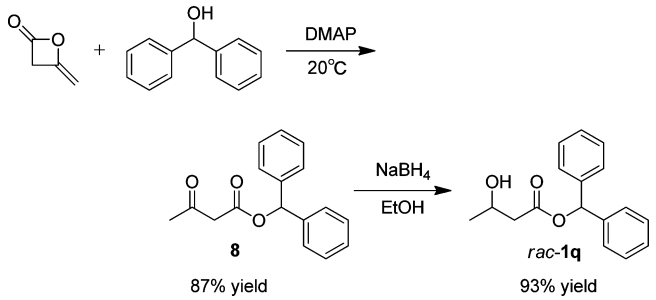
*1. Preparation of Racemic α-Methylene-β-hydroxy Esters 1 (Morita–Baylis–Hillmann reaction).* To a rounded-bottomed flask were added aldehyde (1.2 equiv), DABCO (0.3 equiv), and acrylate ester (1.0 equiv) via syringe, and the resulting homogeneous solution was stirred at room temperature and monitored by TLC. The mixture was extracted with $CH_2Cl_2$ and water, and the combined organic solution was washed with brine, dried over anhydrous $Na_2SO_4$, and concentrated. The crude product was purified by column chromatography on silica gel (petroleum/EtOAc = 6/1), to afford the product.



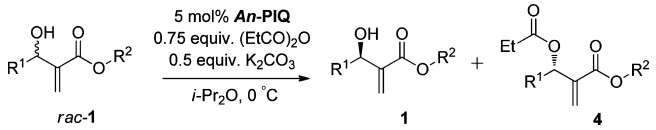

*2. Preparation of Racemic Carboxylates of α-Methylene-β-hydroxy Esters.* To a solution of racemic α-methylene-β-hydroxy ester (1.0 equiv) in *i*-$Pr_2O$ (0.2 M) were added (±)-tetramisole (0.5 equiv), $K_2CO_3$ (1.0 equiv), and $(R^3CO)_2O$ (1.0 equiv). The mixture was stirred at room temperature and monitored by TLC. The mixture was extracted with DCM, and the combined organic phases were washed with brine and concentrated by reduced pressure to get the crude product, which was purified by column chromatography on silica gel (petroleum/EtOAc = 10/1).

*3. Preparation of Benzhydryl 3-Hydroxybutanoate (rac-**1q**).* Compound **8** was prepared according to literature procedures.[16] To a solution of **8** (536.6 mg, 2 mmol) in ethanol (8 mL) at 0 °C was added sodium borohydride (75.7 mg, 2 mmol). The reaction mixture was stirred for 15 min at 0 °C, and then saturated aqueous ammonium chloride was added. The mixture was extracted with DCM (3 × 30 mL), and the organic layer was washed with brine (20 mL) and dried over sodium sulfate. After filtration and evaporation, the crude product was purified by column chromatography (petroleum/EtOAc = 8/1) to afford the product *rac*-**1q**.




*4. General Procedure for Nonenzymatic Resolution of Racemic α-Methylene-β-hydroxy Esters **1** with An-PIQ.* Under an atmosphere of $N_2$, catalyst *An*-PIQ (0.01 mmol), secondary alcohol (0.2 mmol), $K_2CO_3$ (0.1 mmol), and isopropyl ether (2 mL) were sequentially added to a 10 mL flame-dried Schlenk tube in an ice bath. After the mixture was stirred at 0 °C for 5 min, propionyl anhydride (0.15 mmol) was added, the resulting solution was stirred at 0 °C for the specified period and quenched by rapid addition of 0.2 mL of methanol. The solution was warmed to room temperature and stirred for an additional 2 h. The solvent was removed in vacuo and the residue purified by silca gel chromatography (5–10% EtOAc/petroleum) to separate the ester from the unreacted alcohol.




*Benzyl (R)-3-Hydroxy-2-methylenebutanoate (**1a**).*[17] Colorless oil (15.7 mg, 38% yield), $^1$H NMR (400 MHz, $CDCl_3$): δ 7.44–7.29 (m, 5H), 6.27 (s, 1H), 5.85 (s, 1H), 5.23 (s, 2H), 4.74–4.59 (m, 1H), 2.68 (s, 1H), 1.39 (d, *J* = 6.3 Hz, 3H). The ee was determined by HPLC (Chiralcel IF, 1 mL/min, 90/10 hexane/*i*-PrOH, λ = 254 nm, retention time: (*R*) 7.55 min, (*S*) 8.49 min.

*Benzhydryl (R)-3-Hydroxy-2-methylenebutanoate (**1b**).* Colorless oil (26.5 mg, 47% yield), $^1$H NMR (400 MHz, $CDCl_3$): δ 7.47–7.26 (m, 10H), 6.96 (s, 1H), 6.39 (s, 1H), 5.90 (s, 1H), 4.71–4.62 (m, 1H), 2.60 (d, *J* = 5.5 Hz, 1H), 1.39 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 165.6, 143.9, 140.0, 128.6, 128.1, 127.0(6),


DOI: 10.1021/acs.joc.5b00073
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127.0(5), 124.4, 77.5, 67.0, 22.2; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{18}H_{18}O_3$: 282.1256, found: 282.1255. (*R*)-**1b**: $[\alpha]^{25}_D$ = +14.6° (*c* 0.01, $CHCl_3$) (99.1% ee). The ee was determined by HPLC (Chiralcel OJ, 1 mL/min, 80/20 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 18.78 min, (*S*) 23.69 min.

*Benzhydryl (R)-3-Hydroxy-2-methylenepentanoate (**1c**).* Colorless oil (28.4 mg, 48% yield), $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.39−7.26 (m, 10H), 6.94 (s, 1H), 6.41 (s, 1H), 5.88 (s, 1H), 4.38 (m, 1H), 2.49 (d, *J* = 6.6 Hz, 1H), 1.79−1.56 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 164.5, 141.6, 139.0, 138.9(8), 127.6, 127.0, 126.0(1), 126.0(0), 124.3, 76.4, 71.9, 28.2, 9.0; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{19}H_{20}O_3$: 296.1412, found: 296.1413. (*R*)-**1c**: $[\alpha]^{25}_D$ = +11.9° (c 0.01, CHCl3) (96.5% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 40/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 16.89 min, (*R*) 19.82 min.

*Benzhydryl (R)-3-Hydroxy-2-methylenehexanoate (**1d**).* Colorless oil (28.5 mg, 46% yield), $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.45−7.27 (m, 10H), 6.95 (s, 1H), 6.39 (s, 1H), 5.87 (s, 1H), 4.53−4.38 (m, 1H), 2.48 (d, *J* = 5.7 Hz, 1H), 1.70−1.54 (m, 2H), 1.53−1.27 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H);$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.6, 143.0, 140.0, 139. 9(9), 128.6, 128.0, 127.1, 127.0, 125.1, 77.4, 71.4, 38.5, 19.0, 13.8; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{20}H_{22}O_3$: 310.1569, found: 310.1571. (*R*)-**1d**: $[\alpha]^{25}_D$ = +13.9° (*c* 0.01, $CHCl_3$) (99.6% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 40/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 14.36 min, (*R*) 16.92 min.

*Benzhydryl (R)-3-Hydroxy-2-methyleneheptanoate (**1e**).* White solid (30.5 mg, 47% yield), mp 42−43 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.41−7.27 (m, 10H), 6.95 (s, 1H), 6.39 (s, 1H), 5.88 (s, 1H), 4.49−4.40 (m, 1H), 2.47 (d, *J* = 6.6 Hz, 1H), 1.74−1.60 (m, 2H), 1.48−1.21 (m, 4H), 0.87 (t, *J* = 6.9 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.6, 143.0, 140.0, 139.9(8), 128.6, 128.0, 127.1, 127.0, 125.1, 77.4, 71.7, 36.0, 28.0, 22.5, 14.0; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{21}H_{24}O_3$: 324.1725, found: 324.1724. (*R*)-**1e**: $[\alpha]^{25}_D$ = +13.7° (*c* 0.01, $CHCl_3$) (98.3% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 40/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 13.60 min, (*R*) 15.99 min.

*Benzhydryl (R)-3-Hydroxy-5-methyl-2-methylenehexanoate (**1f**).* White solid (29.8 mg, 46% yield), mp 50−51 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44−7.17 (m, 10H), 6.95 (s, 1H), 6.38 (s, 1H), 5.89 (s, 1H), 4.59−4.46 (m, 1H), 2.48 (s, 1H), 1.86−1.71 (m, 1H), 1.61−1.49 (m, 1H), 1.49−1.35 (m, 1H), 0.91 (d, *J* = 6.1 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.6, 143.3, 140.0, 139.9, 128.6, 128.1, 127.1, 127.0, 125.1, 77.4, 69.9, 45.5, 24.8, 23.3, 21.8; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{21}H_{24}O_3$: 324.1725, found: 324.1726. (*R*)-**1f**: $[\alpha]^{25}_D$ = +22.0° (*c* 0.01, $CHCl_3$) (99.9% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 100/5 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 16.75 min, (*S*) 19.62 min.

*Benzhydryl (R)-3-Hydroxy-4-methyl-2-methylenepentanoate (**1g**).* Colorless oil (36.6 mg, 59% yield), $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44−7.26 (m, 10H), 6.93 (s, 1H), 6.43 (s, 1H), 5.84 (s, 1H), 4.17−4.09 (m, 1H), 2.45 (d, *J* = 7.6 Hz, 1H), 1.96−1.85 (m, 1H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.7, 141.8, 140.1, 140.0, 128.6, 128.0, 127.0(2), 127.0(1), 126.2, 77.5, 77.4, 32.7, 19.6, 17.4; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{20}H_{22}O_3$: 310.1569, found: 310.1568. (*R*)-**1g**: $[\alpha]^{25}_D$ = +7.1° (*c* 0.01, $CHCl_3$) (62.9% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 100/5 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 18.17 min, (*S*) 20.51 min.

*Benzhydryl (R)-2-(Cyclohexyl(hydroxy)methyl)acrylate (**1h**).* White solid (39.9 mg, 57% yield), mp 87−89 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.42−7.27 (m, 10H), 6.93 (s, 1H), 6.40 (s, 1H), 5.80 (s, 1H), 4.16−4.08 (m, 1H), 2.43 (d, *J* = 7.8 Hz, 1H), 1.96−1.86 (m, 1H), 1.73−1.50 (m, 5H), 1.23−0.83 (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.7, 141.6, 140.0, 139.9(6), 128.6, 128.0, 127.0, 126.2, 77.4, 77.1, 42.5, 30.0, 28.1, 26.4, 26.1, 25.9; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{23}H_{26}O_3$: 350.1882, found: 350.1884. (*R*)-**1h**: $[\alpha]^{25}_D$ = +5.7° (*c* 0.01, $CHCl_3$) (61.4% ee). The ee was determined by HPLC (Chiralcel OJ, 1 mL/min, 80/20 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 10.02 min, (*R*) 14.33 min.

*Benzhydryl (R)-3-Hydroxy-2-methylene-5-phenylpentanoate (**1i**).* Colorless oil (33.5 mg, 45% yield), $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.36−7.14 (m, 15H), 6.95 (s, 1H), 6.41 (s, 1H), 5.89 (s, 1H), 4.52−4.43 (m, 1H), 2.85−2.57 (m, 2H), 2.54 (d, *J* = 6.3 Hz, 1H), 2.01−1.86 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.5, 142.8, 141.6, 140.0, 139.9, 128.6, 128.5, 128.4, 128.0(8), 128.0(6), 127.1, 127.0, 125.9, 125.5, 77.5, 70.9, 37.8, 32.1; HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{25}H_{24}O_3Na$: 395.1623, found: 395.1622. (*R*)-**1i**: $[\alpha]^{25}_D$ = +17.6° (*c* 0.01, $CHCl_3$) (99.4% ee). The ee was determined by HPLC (Chiralcel OJ, 1 mL/min, 80/20 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 23.74 min; (*R*) 30.76 min.

*Methyl (R)-3-Hydroxy-2-methylene-5-phenylpentanoate (**1j**).* Colorless oil (22.9 mg, 52% yield), $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.31−7.15 (m, 5H), 6.24 (s, 1H), 5.81 (s, 1H), 4.46−4.38 (m, 1H), 3.78 (s, 3H), 2.89−2.68 (m, 2H), 2.64 (d, *J* = 6.7 Hz, 1H), 2.03−1.94 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.6, 143.3, 140.0, 139.9, 128.6, 128.1, 127.1, 127.0, 125.1, 77.4, 69.9, 45.5, 24.8, 23.3, 21.8; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{13}H_{16}O_3$: 220.1099, found: 220.1101. (*R*)-**1j**: $[\alpha]^{25}_D$ = +24.9° (*c* 0.01, $CHCl_3$) (72.1% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 90/10 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 6.76 min, (*S*) 8.08 min.

*Naphthalen-1-ylmethyl (R)-3-Hydroxy-2-methylenebutanoate (**1k**).* Colorless oil (29.2 mg, 57% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.02 (d, *J* = 8.2 Hz, 1H), 7.93−7.84 (m, 2H), 7.60−7.42 (m, 4H), 6.23 (s, 1H), 5.82 (s, 1H), 5.68 (s, 2H), 4.68−4.59 (m, 1H), 2.63 (d, *J* = 5.6 Hz, 1H), 1.38 (d, *J* = 6.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 166.5, 143.6, 133.8, 131.7, 131.2, 129.5, 128.8, 127.5, 126.7, 126.0, 125.3, 124.5, 123.4, 67.0, 65.0, 22.2; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{16}H_{16}O_3$: 256.1099, found: 256.1100. (*R*)-**1k**: $[\alpha]^{25}_D$ = +7.8° (*c* 0.01, $CHCl_3$) (61.8% ee). The ee was determined by HPLC (Chiralcel OD, 1 mL/min, 90/10 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 10.11 min, (*S*) 11.24 min.

*Phenethyl (R)-3-Hydroxy-2-methylenebutanoate (**1l**).* Colorless oil (23.3 mg, 53% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.43−7.13 (m, 5H), 6.19 (s, 1H), 5.80 (s, 1H), 4.45−4.36 (m, 1H), 4.40 (t, *J* = 6.6 Hz, 2H), 3.00 (t, *J* = 6.6 Hz, 2H), 2.57 (s, 1H), 1.35 (d, *J* = 6.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 166.5, 143.7, 137.7, 128.8, 128.6, 126.7, 124.1, 67.0, 65.3, 35.1, 22.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{13}H_{16}O_3$: 220.1099, found: 220.1106. (*R*)-**1l**: $[\alpha]^{25}_D$ = +9.9° (*c* 0.01, $CHCl_3$) (81.3% ee). The ee was determined by HPLC (Chiralcel IF, 1 mL/min, 90/10 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 7.58 min, (*S*) 11.70 min.

*Benzhydryl (S)-4-(Benzyloxy)-3-hydroxy-2-methylenebutanoate (**1m**).* Colorless oil (28.7 mg, 37% yield). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36−7.26 (m, 15H), 6.93 (s, 1H), 6.52 (s, 1H), 6.09 (s, 1H), 4.84−4.76 (m, 1H), 4.53 (s, 2H), 3.72 (dd, *J* = 9.6, 3.4 Hz, 1H), 3.40 (dd, *J* = 9.6, 7.6 Hz, 1H), 2.90 (d, *J* = 4.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 163.9, 139.0, 138.9, 138.3, 136.8, 127.5(6), 127.5(5), 127.5, 127.0, 126.9(8), 126.8, 126.7, 126.0(9), 126.0(7), 126.0, 76.4, 72.6, 72.3, 68.5; HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{25}H_{24}O_4Na$: 411.1572, found: 411.1570. (*S*)-**1m**: $[\alpha]^{25}_D$ = +9.1° (*c* 0.01, $CHCl_3$) (55.4% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 60/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 28.68 min, (*S*) 32.58 min.

*Benzhydryl (S)-4-((tert-Butyldimethylsilyl)oxy)-3-hydroxy-2-methylenebutanoate (**1n**).* Colorless oil (41.2 mg, 50% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.41−7.25 (m, 10H), 6.96 (s, 1H), 6.52 (s, 1H), 6.07 (s, 1H), 4.65−4.59 (m, 1H), 3.86 (dd, *J* = 10.0, 3.8 Hz, 1H), 3.46 (dd, *J* = 10.0, 6.5 Hz, 1H), 2.98 (d, *J* = 4.9 Hz, 1H), 0.87 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 164.9, 140.1, 140.0, 139.5, 128.6, 128.5, 128.0, 127.9(6), 127.2, 127.0, 126.9, 77.3, 70.8, 66.4, 25.9, 18.3, −5.4(0), −5.4(3); HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{24}H_{32}O_4NaSi$: 435.1968, found: 435.1968. (*S*)-**1n**: $[\alpha]^{25}_D$ = +19.4° (*c* 0.01, $CHCl_3$) (98.3% ee). The ee was determined by HPLC (Chiralcel OD, 1 mL/min, 40/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 6.08 min, (*R*) 7.65 min.

*Benzhydryl (R)-5-(Benzyloxy)-3-hydroxy-2-methylenepentanoate (**1o**).* Colorless oil (31.4 mg, 39% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.55−7.18 (m, 15H), 6.93 (s, 1H), 6.45 (s, 1H), 6.05−6.00 (m, 1H), 4.84−4.68 (m, 1H), 4.51 (s, 2H), 3.77−3.61 (m, 2H), 3.60


DOI: 10.1021/acs.joc.5b00073
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(d, $J$ = 4.8 Hz, 1H), 2.13−1.96 (m, 1H), 1.96−1.74 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.3, 142.5, 140.1, 137.9, 128.6, 128.5, 128.0, 127.9(8), 127.8, 127.7(6), 127.1, 127.0, 125.5, 77.3, 73.4, 70.2, 68.6, 35.8; HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{26}H_{26}O_4Na$: 425.1729, found: 425.1729. ($R$)-**1o**: $[\alpha]^{25}_D$ = +18.6° ($c$ 0.01, $CHCl_3$) (99.8% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 100/5 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 13.37 min; ($R$) 15.04 min.

*Benzhydryl (R)-5-((tert-Butyldimethylsilyl)oxy)-3-hydroxy-2-methylenepentanoate (**1p**).* Colorless oil (40.9 mg, 48% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44−7.27 (m, 10H), 6.93 (s, 1H), 6.47 (s, 1H), 6.10−6.02 (m, 1H), 4.84−4.68 (m, 1H), 4.01 (d, $J$ = 4.1 Hz, 1H), 3.94−3.73 (m, 2H), 2.01−1.86 (m, 1H), 1.78−1.64 (m, 1H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07(5) (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 165.2, 142.6, 140.2, 128.5(6), 128.5(5), 128.0, 127.9, 127.1, 127.0, 125.3, 77.2, 70.6, 62.2, 37.7, 25.9, 18.1, −5.5, −5.6; HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{25}H_{34}O_4NaSi$: 449.2124, found: 449.2122. ($R$)-**1p**: $[\alpha]^{25}_D$ = +20.9° ($c$ 0.01, $CHCl_3$) (99.7% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 40/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 11.58 min, ($R$) 12.64 min.

*Benzhydryl (R)-3-Hydroxybutanoate (**1q**).* White solid (29.2 mg, 54% yield), mp 45−46 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.42−7.26 (m, 10H), 6.91 (s, 1H), 4.27−4.16 (m, 1H), 2.87 (d, $J$ = 3.7 Hz, 1H), 2.62 (dd, $J$ = 16.5, 3.7 Hz, 1H), 2.55 (dd, $J$ = 16.5, 8.5 Hz, 1H), 1.22 (d, $J$ = 6.3 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 171.8, 140.0, 139.9, 128.5(9), 128.5(8), 128.1, 128.0, 127.2, 127.1, 77.3, 64.3, 43.2, 22.5; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{17}H_{18}O_3$: 270.1256, found: 270.1258. ($R$)-**1q**: $[\alpha]^{25}_D$ = −15.5° ($c$ 0.01, $CHCl_3$) (70.7% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 90/10 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 9.68 min, ($R$) 17.48 min.

*Benzyl (S)-3-(Isobutyryloxy)-2-methylenebutanoate (**2a**).* Colorless oil (24.3 mg, 44% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44−7.30 (m, 5H), 6.35 (s, 1H), 5.86 (s, 1H), 5.75 (q, $J$ = 6.5 Hz, 1H), 5.31−5.16 (m, 2H), 2.61−2.51 (m, 1H), 1.42 (d, $J$ = 6.5 Hz, 3H), 1.17 (dd, $J$ = 6.8, 5.3 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 174.7, 164.1, 140.3, 134.7, 127.6, 127.2, 127.1, 123.8, 66.8, 65.6, 33.0, 19.1, 17.9, 17.8; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{16}H_{20}O_4$: 276.1362, found: 276.1368.

*Benzhydryl (S)-3-(Isobutyryloxy)-2-methylenebutanoate (**2b**).* White solid (35.2 mg, 50% yield), mp 53−54 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.41−7.22 (m, 10H), 6.96 (s, 1H), 6.41 (s, 1H), 5.87 (s, 1H), 5.83−5.74 (m, 1H), 2.56−2.45 (m, 1H), 1.40 (d, $J$ = 6.2 Hz, 3H), 1.19−1.05 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 174.7, 163.3, 140.3, 139.0, 127.5, 127.0, 126.9, 126.1, 126.0, 124.2, 76.5, 66.9, 33.0, 19.0, 17.8; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{22}H_{24}O_4$: 352.1675, found: 352.1676. ($S$)-**2b**: $[\alpha]^{25}_D$ = −15.1° ($c$ 0.01, $CHCl_3$) (90.2% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 100/5 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 9.47 min, ($R$) 10.84 min.

*Benzhydryl (S)-3-Acetoxy-2-methylenebutanoate (**5b**).* Colorless oil (33.1 mg, 51% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.36−7.29 (m, 10H), 6.97 (s, 1H), 6.42 (s, 1H), 5.88 (s, 1H), 5.84−5.75 (m, 1H), 2.00 (s, 3H), 1.41 (d, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 168.8, 163.3, 140.1, 139.0, 138.9, 127.5, 127.0, 126.0(8), 126.0(6), 124.5, 76.5, 67.2, 20.1, 18.9; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{20}H_{20}O_4$: 324.1362, found: 324.1365. ($S$)-**5b**: $[\alpha]^{25}_D$ = −11.9° ($c$ 0.01, $CHCl_3$) (84.2% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 40/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($R$) 12.95 min, ($S$) 13.96 min.

*Benzhydryl (S)-2-Methylene-3-(propionyloxy)butanoate (**4b**).* Colorless oil (34.5 mg, 51% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.41−7.22 (m, 10H), 6.97 (s, 1H), 6.41 (s, 1H), 5.87 (s, 1H), 5.85−5.76 (m, 1H), 2.40−2.15 (m, 2H), 1.41 (d, $J$ = 6.4 Hz, 3H), 1.10 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.1, 163.3, 140.2, 138.9(9), 138.9(5), 127.5, 127.0, 126.9, 126.0(7), 126.0(5), 124.4, 76.5, 67.0, 26.7, 18.9, 8.0; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{21}H_{22}O_4$: 338.1518, found: 338.1516. ($S$)-**4b**: $[\alpha]^{25}_D$ = −10.7° ($c$ 0.01, $CHCl_3$) (88.5% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 40/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 13.88 min, ($R$) 15.80 min.

*Benzhydryl (S)-2-Methylene-3-(propionyloxy)pentanoate (**4c**).* Colorless oil (35.2 mg, 50% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.39−7.27 (m, 10H), 6.95 (s, 1H), 6.42 (s, 1H), 5.81 (s, 1H), 5.70−5.62 (m, 1H), 2.40−2.27 (m, 2H), 1.89−1.76 (m, 1H), 1.76−1.63 (m, 1H), 1.13 (t, $J$ = 7.5 Hz, 3H), 0.88 (t, $J$ = 7.3 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.3, 163.4, 139.1, 139.0(3), 139.0(1), 127.5, 127.0, 126.9, 126.1, 126.0, 124.8, 76.5, 71.6, 26.7, 26.1, 8.5, 8.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{22}H_{24}O_4$: 352.1675, found: 352.1680. ($S$)-**4c**: $[\alpha]^{25}_D$ = −14.8° ($c$ 0.01, $CHCl_3$) (89.9% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 40/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 15.68 min, ($R$) 20.30 min.

*Benzhydryl (S)-2-Methylene-3-(propionyloxy)hexanoate (**4d**).* Colorless oil (38.1 mg, 52% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.51−7.27 (m, 10H), 6.96 (s, 1H), 6.40 (s, 1H), 5.81 (s, 1H), 5.78−5.66 (m, 1H), 2.39−2.23 (m, 2H), 1.78−1.62 (m, 2H), 1.45−1.28 (m, 2H), 1.13 (t, $J$ = 7.5 Hz, 3H), 0.87 (t, $J$ = 7.3 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.3, 163.4, 139.5, 139.0(2), 139.0(0), 127.5, 127.0, 126.9, 126.2, 126.0, 124.5, 76.5, 70.5, 35.4, 26.7, 17.7, 12.7, 8.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{23}H_{26}O_4$: 366.1831, found: 366.1833. ($S$)-**4d**: $[\alpha]^{25}_D$ = −14.2° ($c$ 0.01, $CHCl_3$) (85.3% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 60/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 17.60 min, ($R$) 19.54 min.

*Benzhydryl (S)-2-Methylene-3-(propionyloxy)heptanoate (**4e**).* Colorless oil (38.0 mg, 50% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44−7.26 (m, 10H), 6.96 (s, 1H), 6.39 (s, 1H), 5.80 (s, 1H), 5.70 (dd, $J$ = 7.7, 4.7 Hz, 1H), 2.43−2.22 (m, 2H), 1.82−1.61 (m, 2H), 1.30−1.23 (m, 4H), 1.13 (t, $J$ = 7.6 Hz, 3H), 0.84 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.3, 163.4, 139.5, 139.0, 138.9(9), 127.5, 127.0, 126.9, 126.2, 126.0, 124.6, 76.5, 70.8, 33.0, 26.7, 26.5, 21.3, 12.9, 8.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{24}H_{28}O_4$: 380.1988, found: 380.1989. ($S$)-**4e**: $[\alpha]^{25}_D$ = −12.1° ($c$ 0.01, $CHCl_3$) (89.1% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 99.5/0.5 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 4.87 min, ($R$) 8.10 min.

*Benzhydryl (S)-5-Methyl-2-methylene-3-(propionyloxy)-hexanoate (**4f**).* Colorless oil (38.8 mg, 51% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.46−7.26 (m, 10H), 6.96 (s, 1H), 6.38 (s, 1H), 5.85−5.72 (m, 2H), 2.44−2.23 (m, 2H), 1.65−1.51 (m, 3H), 1.13 (t, $J$ = 7.6 Hz, 3H), 0.93−0.81 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.3, 163.3, 140.0, 138.9(8), 138.9(7), 127.5, 127.0, 126.9, 126.2, 125.9, 124.4, 76.5, 69.4, 42.6, 26.7, 23.9, 22.1, 20.7, 8.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{24}H_{28}O_4$: 380.1988, found: 380.1989. ($S$)-**4f**: $[\alpha]^{25}_D$ = −23.6° ($c$ 0.01, $CHCl_3$) (84.2% ee). The ee was determined by HPLC (Chiralcel AS, 0.8 mL/min, 60/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 5.10 min, ($R$) 6.37 min.

*Benzhydryl (S)-4-Methyl-2-methylene-3-(propionyloxy)-pentanoate (**4g**).* Colorless oil (29.3 mg, 40% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.50−7.27 (m, 10H), 6.94 (s, 1H), 6.43 (d, $J$ = 0.9 Hz, 1H), 5.76 (t, $J$ = 1.0 Hz, 1H), 5.54 (dd, $J$ = 5.6, 0.7 Hz, 1H), 2.44−2.28 (m, 2H), 2.14−2.01 (m, 1H), 1.14 (t, $J$ = 7.6 Hz, 3H), 0.90−0.84 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.3, 163.4, 139.1, 139.0, 138.6, 127.5, 127.0, 126.9, 126.2, 125.9, 125.4, 76.5, 75.1, 30.3, 26.7, 18.0, 16.0, 8.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{23}H_{26}O_4$: 366.1831, found: 366.1834. ($S$)-**4g**: $[\alpha]^{25}_D$ = −9.7° ($c$ 0.01, $CHCl_3$) (91.0% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 40/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 16.18 min, ($R$) 19.45 min.

*Benzhydryl (S)-2-(Cyclohexyl(propionyloxy)methyl)acrylate (**4h**).* White solid (33.3 mg, 41% yield), mp 70−71 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.45−7.28 (m, 10H), 6.95 (s, 1H), 6.42 (s, 1H), 5.75 (s, 1H), 5.52 (d, $J$ = 5.8 Hz, 1H), 2.41−2.28 (m, 2H), 1.79−1.48 (m, 6H), 1.19−1.06 (m, 6H), 1.03−0.91 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.4, 163.5, 139.1, 139.0, 138.3, 127.5, 127.0, 126.9, 126.2, 125.9, 125.6, 76.5, 74.8, 39.9, 28.5, 26.7(1), 26.6(7), 25.2, 25.0, 24.9, 8.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{26}H_{30}O_4$: 406.2144, found: 406.2145. The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 40/1 hexane/$i$-PrOH, $\lambda$ = 254 nm, retention time: ($S$) 18.74 min, ($R$) 22.91 min.

*Benzhydryl (S)-2-Methylene-5-phenyl-3-(propionyloxy)-pentanoate (**4i**).* White solid (44.5 mg, 52% yield), mp 43−45 °C.



DOI: 10.1021/acs.joc.5b00073
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$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44−7.04 (m, 16H), 6.96 (s, 1H), 6.43 (s, 1H), 5.83 (s, 1H), 5.79−5.72 (m, 1H), 2.71−2.57 (m, 2H), 2.40−2.25 (m, 2H), 2.19−1.91 (m, 2H), 1.14 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.2, 163.2, 140.1, 139.1, 138.9(4), 138.8(9), 127.5, 127.4, 127.3, 127.0, 126.9, 126.2, 125.9, 124.9, 76.5, 70.4, 34.8, 30.8, 26.6, 8.1; HRMS (ESI-TOF): Calcd for $[M + NH_4]^+$ $C_{28}H_{32}NO_4$: 446.2331, found: 446.2335. (*S*)-**4i**: $[\alpha]^{25}_D$ = −13.0° (*c* 0.01, $CHCl_3$) (82.6% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 99.5/0.5 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 9.33 min, (*R*) 13.71 min.

*Methyl (S)-2-Methylene-5-phenyl-3-(propionyloxy)pentanoate (**4j**).* Colorless oil (25.9 mg, 47% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.42−7.03 (m, 5H), 6.30 (s, 1H), 5.78 (s, 1H), 5.67 (dd, $J$ = 8.1, 4.0 Hz, 1H), 3.76 (s, 3H), 2.81−2.57 (m, 2H), 2.35 (dd, $J$ = 15.1, 7.6 Hz, 2H), 2.15−1.96 (m, 2H), 1.15 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.3, 164.7, 140.2, 139.1, 127.4, 127.3, 125.0, 124.2, 70.3, 50.9, 34.9, 30.7, 26.7, 8.1; HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{16}H_{20}O_4Na$: 299.1259, found: 299.1258. (*S*)-**4j**: $[\alpha]^{25}_D$ = +16.2° (*c* 0.01, $CHCl_3$) (79.1% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 60/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 5.74 min, (*R*) 6.70 min.

*Naphthalen-1-ylmethyl (S)-2-Methylene-3-(propionyloxy)-butanoate (**4k**).* Colorless oil (25.6 mg, 41% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03 (d, $J$ = 8.2 Hz, 1H), 7.94−7.81 (m, 2H), 7.62−7.40 (m, 4H), 6.29 (s, 1H), 5.81 (s, 1H), 5.74 (q, $J$ = 6.4 Hz, 1H), 5.67 (s, 2H), 2.37−2.17 (m, 2H), 1.37 (d, $J$ = 6.4 Hz, 3H), 1.09 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl3): $\delta$ 172.1, 164.2, 140.2, 132.7, 130.6, 130.2, 128.3, 127.7, 126.5, 125.6, 124.9, 124.2, 124.1, 122.5, 67.0, 63.9, 26.7, 19.1, 8.0; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{19}H_{20}O_4$: 312.1362, found: 312.1363. (*S*)-**4k**: $[\alpha]^{25}_D$ = −14.9° (*c* 0.03, $CHCl_3$) (84.0% ee). The ee was determined by HPLC (Chiralcel IF, 1 mL/min, 80/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 14.27 min, (*S*) 15.81 min.

*Phenethyl (S)-2-Methylene-3-(propionyloxy)butanoate (**4l**).* Colorless oil (24.9 mg, 45% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44−7.14 (m, 5H), 6.24 (s, 1H), 5.79 (s, 1H), 5.74−5.65 (m, 1H), 4.38 (t, $J$ = 6.7 Hz, 2H), 2.99 (t, $J$ = 6.7 Hz, 2H), 2.33 (q, $J$ = 7.5 Hz, 2H), 1.34 (d, $J$ = 6.3 Hz, 3H), 1.14 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$):$\delta$ 172.1, 164.2, 140.4, 136.7, 127.9, 127.5, 125.6, 123.6, 67.0, 64.4, 34.1, 26.8, 19.2, 8.1; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{16}H_{20}O_4$: 276.1362, found: 276.1353. (*S*)-**4l**: $[\alpha]^{25}_D$ = −11.9° (*c* 0.01, $CHCl_3$) (90.4% ee). The ee was determined by HPLC (Chiralcel IF, 1 mL/min, 90/10 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 5.42 min, (*S*) 6.16 min.

*Benzhydryl (R)-4-(Benzyloxy)-2-methylene-3-(propionyloxy)-butanoate (**4m**).* Colorless oil (54.2 mg, 61% yield). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34−7.11 (m, 15H), 6.87 (s, 1H), 6.43 (s, 1H), 6.00−5.91 (m, 2H), 4.42 (dd, $J$ = 36.0, 12.2 Hz, 2H), 3.65−3.53 (m, 2H), 2.39−2.20 (m, 2H), 1.07 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.2, 163.0, 138.9, 136.9, 136.1, 127.5, 127.3, 127.0, 126.9, 126.6(1), 126.5(5), 126.5(3), 126.2, 126.0, 76.6, 72.0, 69.9, 69.5, 26.6, 8.0; HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{28}H_{28}O_5Na$: 467.1834, found: 467.1834. (*R*)-**4m**: $[\alpha]^{25}_D$ = −3.2° (*c* 0.01, $CHCl_3$) (29.4% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 90/10 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 5.42 min, (*S*) 6.96 min.

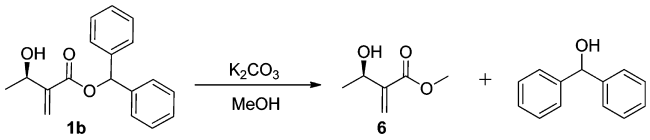
*Benzhydryl (R)-4-((tert-Butyldimethylsilyl)oxy)-2-methylene-3-(propionyloxy)butanoate (**4n**).* Colorless oil (45.9 mg, 49% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.45−7.26 (m, 10H), 6.97 (s, 1H), 6.49 (s, 1H), 5.91 (s, 1H), 5.79 (dd, $J$ = 6.2, 3.5 Hz, 1H), 3.84 (dd, $J$ = 11.1, 3.5 Hz, 1H), 3.72 (dd, $J$ = 11.1, 6.2 Hz, 1H), 2.44−2.28 (m, 2H), 1.14 (t, $J$ = 7.6 Hz, 3H), 0.84 (s, 9H), −0.01 (s, 3H), −0.02 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.1, 163.1, 139.0, 136.2, 127.5(2), 127.5(1), 127.0, 126.9, 126.7, 126.2, 126.0, 76.5, 71.6, 63.1, 26.7, 24.7, 17.2, 8.0, −6.4(6), −6.4(7); HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{27}H_{36}O_5NaSi$: 491.2230, found: 491.2229. (*R*)-**4n**: $[\alpha]^{25}_D$ = −1.1° (*c* 0.02, $CHCl_3$) (78.1% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 100/5 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 5.36 min, (*R*) 6.05 min.

*Benzhydryl (S)-5-(Benzyloxy)-2-methylene-3-(propionyloxy)-pentanoate (**4o**).* Colorless oil (54.0 mg, 59% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.48−7.22 (m, 15H), 6.95 (s, 1H), 6.40 (s, 1H), 5.87 (dd, $J$ = 8.5, 4.1 Hz, 1H), 5.83 (s, 1H), 4.48−4.37 (m, 2H), 3.59−3.37 (m, 2H), 2.36−2.20 (m, 2H), 2.18−2.07 (m, 1H), 2.06−1.93 (m, 1H), 1.09 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.1, 163.2, 139.1, 139.0, 137.3, 127.5, 127.3, 126.9(4), 126.8(8), 126.6, 126.5, 126.1, 125.9, 125.1, 76.5, 71.9, 68.5, 65.3, 33.4, 26.6, 8.0; HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{29}H_{30}O_5Na$: 481.1991, found: 481.1992. (*S*)-**4o**: $[\alpha]^{25}_D$ = −7.9° (*c* 0.03, $CHCl_3$) (52.5% ee). The ee was determined by HPLC (Chiralcel AS, 1 mL/min, 100/5 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) (*S*) 5.68 min, 6.46 min.

*Benzhydryl (S)-5-((tert-Butyldimethylsilyl)oxy)-2-methylene-3-(propionyloxy)pentanoate (**4p**).* Colorless oil (48.2 mg, 50% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.43−7.27 (m, 10H), 6.97 (s, 1H), 6.41 (s, 1H), 5.88−5.79 (m, 2H), 3.74−3.55 (m, 2H), 2.43−2.21 (m, 2H), 2.10−1.81 (m, 2H), 1.12 (t, $J$ = 7.6 Hz, 3H), 0.86 (s, 9H), 0.00 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.1, 163.2, 139.3, 139.0, 127.5, 126.9(4), 126.8(7), 126.2, 126.0, 125.1, 76.4, 68.3, 58.3, 36.2, 26.7, 24.9, 17.2, 8.0, −6.4(8), −6.5(1); HRMS (ESI-TOF): Calcd for $[M + Na]^+$ $C_{28}H_{38}O_5NaSi$: 505.2386, found: 505.2387. (*S*)-**4p**: $[\alpha]^{25}_D$ = −3.6° (*c* 0.01, $CHCl_3$) (85.1% ee). The ee was determined by HPLC (Chiralcel AD, 1 mL/min, 40/1 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*R*) 5.60 min, (*S*) 6.46 min.

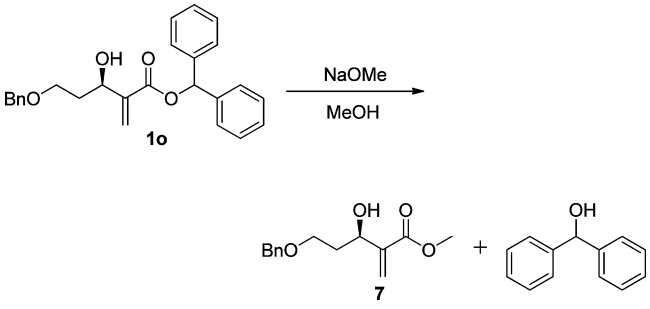
*Benzhydryl (S)-3-(Propionyloxy)butanoate (**4q**).* Colorless oil (29.3 mg, 45% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.41−7.22 (m, 10H), 6.90 (s, 1H), 5.38−5.28 (m, 1H), 2.75 (dd, $J$ = 15.5, 8.0 Hz, 1H), 2.62 (dd, $J$ = 15.5, 5.3 Hz, 1H), 2.24−1.99 (m, 2H), 1.28 (d, $J$ = 6.3 Hz, 3H), 1.01 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.5, 168.2, 139.0, 127.5, 126.9, 126.1(4), 126.1(0), 76.1, 66.2, 40.1, 26.6, 18.9, 7.9; HRMS (EI-TOF): Calcd for $[M]^+$ $C_{20}H_{22}O_4$: 326.1518, found: 326.1516. (*S*)-**4q**: $[\alpha]^{25}_D$ = +5.6° (*c* 0.02, $CHCl_3$) (84.0% ee). The ee was determined by HPLC (Chiralcel OJ, 1 mL/min, 90/10 hexane/*i*-PrOH, $\lambda$ = 254 nm, retention time: (*S*) 16.17 min, (*R*) 19.41 min.

*5. Preparation of Methyl Ester (R)-**6** and (R)-**7**.* A mixture of ester **1b** (350 mg, 1.24 mmol) and $K_2CO_3$ (86 mg, 0.62 mmol) in dried




MeOH (6 mL) was stirred at room temperature for 1 h. The reaction mixture was neutralized by the addition of Dowex 50 ($H^+$ form), filtered, concentrated, and purified by silica gel column chromatography (petroleum/EtOAc = 6/1) to give product **6** (130.7 mg, 81%) as a colorless oil.

*Methyl (R)-3-Hydroxy-2-methylenebutanoate (**6**).*[8a] Colorless oil (130.7 mg, 81% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.22 (s, 1H), 5.86−5.80 (m, 1H), 4.67−4.58 (m, 1H), 3.80 (s, 3H), 2.63 (s, 1H), 1.40 (d, $J$ = 6.5 Hz, 3H). (*R*)-**6**: $[\alpha]^{25}_D$ = +17.4° (*c* 0.01, $CHCl_3$) (99.2% ee); ($ee_{1b}$= 99.2%). The ee was determined by HPLC (Chiralcel OD, 1 mL/min, 40/1 hexane/*i*-PrOH, $\lambda$ = 220 nm, retention time: (*R*) 11.68 min, (*S*) 13.36 min.






DOI: 10.1021/acs.joc.5b00073
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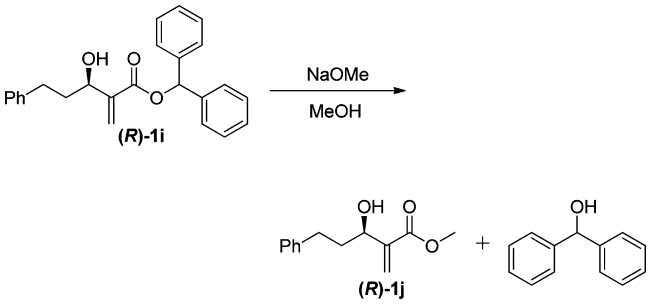
A mixture of ester **1o** (560 mg, 1.39 mmol) and NaOMe (15 mg, 0.28 mmol) in dried MeOH (7 mL) was stirred at room temperature for 4 h. The reaction mixture was neutralized by the addition of Dowex 50 ($H^+$ form), filtered, concentrated, and purified by silica gel column chromatography (petroleum/EtOAc = 6/1) to give product **7** (299.2 mg, 86%) as a colorless oil.

*Methyl (R)-5-(Benzyloxy)-3-hydroxy-2-methylenepentanoate (7).*[9a] Colorless oil (299.2 mg, 86% yield). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40−7.29 (m, 5H), 6.28 (s, 1H), 5.96−5.89 (m, 1H), 4.76−4.63 (m, 1H), 4.52 (s, 2H), 3.75 (s, 3H), 3.72−3.64 (m, 2H), 3.61 (d, $J$ = 5.0 Hz, 1H), 2.12−1.99 (m, 1H), 1.93−1.79 (m, 1H).

*6. Transesterification of (R)-1i.* The procedure of the transesterification of (*R*)-**1i** (74.4 mg, 0.2 mmol) was employed according




to the preparation of compound **7**. (*R*)-**1j**: Colorless oil (35 mg, 80% yield). $[\alpha]^{25}_D$ = +26.8° ($c$ 0.01, $CHCl_3$) (99.6% ee); ($ee_{1i}$ = 99.6%).

## ■ ASSOCIATED CONTENT

### Supporting Information

Copies of $^1$H and $^{13}$C NMR spectra and HPLC data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

### Corresponding Authors

*E-mail: xxyu@ecust.edu.cn.

*E-mail: weiping_deng@ecust.edu.cn.

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

We are grateful for financial support from the Fundamental Research Funds for the Central Universities, the National Natural Science Foundation of China (no. 21372074).

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DOI: 10.1021/acs.joc.5b00073
*J. Org. Chem.* 2015, 80, 3159−3169